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Amendments To the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A compound of the formula I:

I

wherein:

X is selected from the group consisting of:

-NR¹⁰-, -O-, -CH₂O-, -CONR¹⁰-, -NR¹⁰CO-, -CO₂-, -OCO-, -CH₂(NR¹⁰)CO-, -N(COR¹⁰)-, -CH₂N(COR¹⁰)-, phenyl, and C₃₋₆ cycloalkyl,

where R^{10} is independently selected from: hydrogen, $C_{1\text{-}6}$ alkyl, benzyl, phenyl, and $C_{1\text{-}6}$ alkyl- $C_{3\text{-}6}$ cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl;

W is selected from:

phenyl and heterocycle, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkoxy and trifluoromethyl;

Z is C;

n is an integer selected from 0, 1, 2, 3 and 4;

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R1 is selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₆alkyl,
- (f) C3-7cycloalkyl,
- (g) -O-C₁-6alkyl,
- (h) -O-C3-7cycloalkyl,
- (i) -SCF₃,
- (j) -S-C₁-6alkyl,
- (k) -SO₂-C₁-6alkyl,
- (l) phenyl,
- (m) heterocycle,
- (n) $-CO_2R^9$,
- (o) -CN,
- (p) $-NR^{9}R^{10}$,
- (q) $-NR9-SO_2-R_{10}$,
- (r) $-SO_2-NR^9R^{10}$,
- (s) -CONR9R10
- (t) $-NHC(=NH)NH^2$, and
- (u) hydrogen,

R² is selected from:

(C₀-6alkyl)-phenyl and (C₀-6alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -C₁-3alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,

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- trifluoromethoxy, (c)
- hydroxy, (d)
- C₁-6alkyl, (e)
- (f) C3-7cycloalkyl,
- -O-C₁-6alkyl, (g)
- (h) -O-C3-7cycloalkyl,
- (i) -SCF₃,
- (j) -S-C₁₋₆alkyl,
- (k) -SO₂-C₁-6alkyl,
- phenyl, (l)
- heterocycle, (m)
- $-CO_2R^9$, (n)
- (o) -CN,
- -NR9R10, (p)
- -NR9-SO₂-R10, (q)
- -SO2-NR9R10, and (r)
- -CONR9R10; (s)

R³ is -(C₀-6alkyl)-phenyl,

where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- -O-C₁₋₃alkyl, and (c)
- (d) trifluoromethyl,

and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- trifluoromethyl, (b)
- hydroxy, (c)
- C₁-3alkyl, (d)
- -O-C₁₋₃alkyl, (e)
- -CO₂R⁹, (f)
- (g) -CN,
- -NR9R10, and (h)
- -CONR9R10; (i)

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R4 is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- (d) C₁₋₆alkyl-hydroxy,
- (e) -O-C₁₋₃alkyl,
- (f) $-CO_2R^9$,
- (g) -CONR9R10, and
- (h) -CN;

or where R³ and R⁴ may be joined together to form a ring which is selected from:

- (a) 1H-indene,
- (b) 2,3-dihydro-1H-indene,
- (c) 2,3-dihydro-benzofuran,
- (d) 1,3-dihydro-isobenzofuran,
- (e) 2,3-dihydro-benzothiofuran, and
- (f) 1,3-dihydro-isobenzothiofuran,

or where R³ and R⁵ or R⁴ and R⁶ may be joined together to form a ring which is phenyl,

wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁-3alkyl,
- (e) -O-C₁-3alkyl,
- (f) $-CO_2R^9$,
- (g) -CN,
- (h) -NR9R10, and
- (i) $-CONR^9R^{10}$;

R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C_{1-6} alkyl,
- (d) C₁₋₆alkyl-hydroxy,

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-O-C₁-3alkyl, (e)

(f) oxo, and

halo; (g)

and or a pharmaceutically acceptable salt or salts thereof and individual diastereomer diastereomers thereof.

2. (currently amended) The compound of Claim 1 of the formula Ia:

Ia

and or a pharmaceutically acceptable salt or salts and individual diastereomer diastereomers thereof.

3. (currently amended) The compound of Claim 1 of the formula Ib:

Ib

and or a pharmaceutically acceptable salt or salts and individual diastereomer diastereomers thereof.

4. (currently amended) The compound of Claim 1 of the formula Ic:

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$$R^7$$
 N
 N
 N
 R^2
 N
 R^1

Ic

wherein R7 and R8 are independently selected from:

- (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂H,
- (h) -CO₂C₁₋₃alkyl, and
- (i) -CN;

and or a pharmaceutically acceptable salt or salts and individual diastereomer diastereomers thereof.

5. (currently amended) The compound of Claim 1 of the formula Id:

Id

wherein the dash line represents either single or double bonds; and or a pharmaceutically acceptable salt or salts and individual diastereomer diastereomers thereof.

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6. (currently amended) The compound of Claim 1 of the formula:

$$R^3$$
 R^5
 R^4
 R^6
 N
 N
 R^2
 N
 R^1

wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazolyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, and thiazolyl, and or a pharmaceutically acceptable salt or salts and individual diastereomer diastereomers thereof.

7. (original) The compound of Claim 1 wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and Noxides thereof.

- 8. (original) The compound of Claim 1 wherein X is -CONH-.
- 9. (canceled)
- 10. (previously presented) The compound of Claim 1 wherein n is 0 or 1.
- 11. (original) The compound of Claim 1 wherein R¹ is selected from:
- (a) hydrogen
- (b) halo
- (c) C₁₋₃alkyl,
- (d) -O-C₁-3alkyl,
- (e) $-CO_2R^9$,
- (f) -S-C₁₋₃alkyl,
- (g) -SO₂-C₁-3alkyl,
- (h) -SCF₃,

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- $NHC(=NH)NR^9R^{10}$ (i)
- -NR9R10, (j)
- -NR9-SO₂-R₁₀, (k)
- -SO2-NR9R10, and **(l)**
- -CONR9R10. (m)

12. (original) The compound of Claim 1 wherein R² is selected from -(C₀-4alkyl)-phenyl and -(C₀-4alkyl)-heterocycle,

where heterocycle is selected from:

furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and N-oxides thereof,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- hydroxy, (b)
- -O-C₁₋₃alkyl, and (c)
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- trifluoromethyl, (b)
- trifluoromethoxy, (c)
- (d) hydroxy,
- C₁-3alkyl, (e)
- -O-C₁₋₃alkyl, (f)
- $-CO_2R^9$, (g)
- -S-C₁₋₃alkyl, (h)
- -SO2-C1-3alkyl, (i)
- -SCF₃, (j)
- $-CO_2R^9$, (k)
- -NR9R10 **(1)**
- -NR9-SO2-R10, (m)
- -SO₂-NR⁹R¹⁰, and (n)
- -CONR9R10. (o)

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13. (original) The compound of Claim 1 wherein R² is selected from -(C₀-4alkyl)-phenyl and -(C₀-4alkyl)-heterocycle,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof, where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁-3alkyl,
- (g) -CO₂-C₁-3alkyl,
- (h) -CO₂H,
- (i) -S-C₁₋₃alkyl,
- (j) $-SO_2-C_1$ -3alkyl,
- (k) -SCF₃,
- (l) $-NH_2$,
- (m) -NH-SO₂-C₁-3alkyl, and
- (n) -SO₂-NH₂.

14. (original) The compound of Claim 1 wherein R² is selected from -CH₂-phenyl and -CH₂-heterocycle,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof, and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₃alkyl,

- (f) -O-C₁-3alkyl,
- (g) -CO₂-C₁-3alkyl,
- (h) -CO₂H,
- (i) -S-C₁₋₃alkyl,
- (j) -SO2-C₁₋₃alkyl,
- (k) -SCF₃,
- (1) -NH2,
- (m) -NH-SO₂-C₁₋₃alkyl, and
- (n) -SO₂-NH₂.
- 15. (original) The compound of Claim 1 wherein R² is selected from:
- (1) -CH₂-(phenyl),
- (2) -CH2-(4-bromophenyl),
- (3) -CH₂-(3-chlorophenyl),
- (4) -CH₂-(3,5-difluorophenyl),
- (5) -CH₂-((2-trifluoromethyl)phenyl),
- (6) -CH₂-((3-trifluoromethyl)phenyl),
- (7) -CH2-((4-trifluoromethyl)phenyl),
- (8) -CH₂-((3-trifluoromethoxy)phenyl),
- (9) -CH2-((3-trifluoromethylthio)phenyl),
- (10) -CH2-((3-trifluoromethoxy-5-thiomethyl)phenyl),
- (11) -CH₂-((3-trifluoromethoxy-5-methoxy)phenyl),
- (12) -CH2-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),
- (13) -CH2-((3-trifluoromethoxy-5-amino)phenyl),
- (14) -CH2-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),
- (15) -CH2-((3-trifluoromethoxy-5-sulfonylamino)phenyl),
- (16) -CH₂-((3,5-bis-trifluoromethyl)phenyl),
- (17) -CH₂-((3-fluoro-5-trifluoromethyl)phenyl),
- (18) -CH(CH₃)-((3,5-bis-trifluoromethyl)phenyl),
- (19) -C(CH₃)₂-((3,5-bis-trifluoromethyl)phenyl),
- (20) -CH2-(4-(2-trifluoromethyl)pyridyl),
- (21) -CH2-(5-(3-trifluoromethyl)pyridyl),
- (22) -CH2-(5-(3-trifluoromethyl)pyridazinyl),
- (23) -CH2-(4-(2-trifluoromethyl)pyridyl-N-oxide), and
- (24) -CH2-(5-(3-trifluoromethyl)pyridyl-N-oxide).

16. (original) The compound of Claim 1 wherein R³ is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁₋₃alkyl,
- (e) -O-C₁₋₃alkyl,
- (f) $-CO_2R^9$,
- (g) -CN,
- (h) -NR9R10, and
- (i) $-CONR^9R^{10}$.

17. (original) The compound of Claim 1 wherein R³ is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (c) hydroxy,
- (d) C_{1-3} alkyl,
- (e) -O-C₁-3alkyl, and
- (f) $-CO_2R^9$.

18. (original) The compound of Claim 1 wherein R^3 is phenyl, or para-fluorophenyl.

19. (previously presented) The compound of Claim 1 wherein R^4 is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CO₂H,
- (d) -CO₂C₁-6alkyl, and
- (e) -CN.

20. (original) The compound of Claim 1 wherein R^5 and R^6 are independently selected from:

(a) hydrogen,

(b) hydroxy,

(c) -CH3,

(d) -O-CH3, and

(e) oxo.

21. (canceled)

22. (original) A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

23. (canceled)

24. (canceled)

25. (canceled)

26. (original) A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

27. (new) The compound of Claim 1, which is selected from the group consisting of the following compounds, or a pharmaceutically acceptable salt or individual diastereomer thereof:

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Ex. 11	O F F F F F F F F F F F F F F F F F F F
F N N N-NMe CF ₃ Ex. 31	P 32
F N N N N N CF ₃ Ex. 35	Ex. 32 F O N CF ₃ Ex. 36
Ex. 35 F O N N N CF ₃ Ex. 37	Ex. 38

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O CF ₃ N NH CF ₃ NH ₂	S N N Me H
Ex. 48	Ex. 49
O Me CF ₃ NH ₂ CF ₃	O Me N N CF3
Ex. 50	Ex. 51
N CF ₃ NHAc and Ex. 80	O N N N N NHAC CF ₃